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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/363,100	07/29/1999	DONALD A.G. MICKLE	50074/004003	7723

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CLARK & ELBING LLP
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BOSTON, MA 02110

EXAMINER	
AFREMOVA, VERA	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/363,100	MICKLE ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,2,4-11 and 14-24* is/are pending in the application.

4a) Of the above claim(s) *14-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,4,6,10 and 11* is/are rejected.

7)☐ Claim(s) *2,5 and 7-9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

Claims 1, 2 and 4-11 as amended (12/15/2003) are under examination in the instant office action.

Claims 13 and 25-28 were canceled by applicants (12/26/20031). Claims 3, 12, 29 and 30 were canceled by applicants (4/16/20021). Claims 14-24 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4, 6, 10 and 11 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/03973 for the reasons as explained in the prior office action and below.

Claims are directed to a method for improving heart function in a patient having cardiac scar tissue wherein the method comprises administering to said cardiac scar tissue a cellular suspension containing mesenchymal stem cells (MSC) wherein said administered cells survive in said scar tissue and improve hear function in said patient. Some claims are further drawn to the use of MSC that are isolated from bone marrow, that are cultured prior administration and autologous. Some claims are further drawn to administration of MSC by injection.

WO 99/03973 discloses a method for regeneration and repair of damaged cardiac muscle by administering a cell suspension with MSC into the damaged heart or cardiac myocardium (page 2, lines 29-30; page 3, line 24). The cardiac muscle is damaged through disease or degeneration (page 2, par. 3). The cited patent teaches the use of MSC as a therapy for congestive heart failure (page 2, line 21). Thus, the cited patent encompasses administration of MSC to the same patient having cardiac scar tissue or into the same cardiac scar tissue as encompassed by the presently pending claims and in the light of specification (see specification (from page 1, line 19 to page 2, line 4). The cited patent teaches that the heart environment improves differentiation of MSC into cardiomyocetes (page 10, line 9) and that MSC survive or integrate into surrounding myocardium (page 4, lines 4-6). WO 99/03973 also teaches that MSC are administered by injection (page 3, line 23) and that the administered MSC are obtained from bone marrow (page 3, line 11). The method of the cited patent comprises administration of autologous cells (page 3, line 18). The cited patent also teaches that the administered MSC are cultured prior administration or genetically modified during culturing (page 4, par. 2).

The administered MSC compositions or MSC suspensions are mixtures of cells or co-cultures of unmodified MSC and modified MSC (page 4, par. 3). The cited patent also suggests the use of a partially differentiated mixture containing MSC in order to shorten the time required for complete cell differentiation after administration (page 4, last paragraph) wherein the partially differentiated mixture comprises undifferentiated MSC and differentiated MSC which are cardiomyocetes. Thus, the cited patent teaches administration of co-culture of MSC and cardiomyocetes.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to administer MSC to damaged or cardiac scar tissue for the expected benefits in improving heart function as taught by WO 99/03973. The method of the cited WO 99/03973 is substantially similar, if not identical, to the presently claimed method because it encompasses administration of similar, if not identical, cell suspensions containing MSC. The administered MSC of the cited patent are autologous, derived from bone marrow and cultured or genetically modified. The method of the cited WO 99/03973 is substantially similar, if not identical, to the presently claimed method because it encompasses MSC administration to a similar, if not identical, patient having damaged cardiac tissue including cardiac scar tissue. The cited patent teaches the use of MSC as a therapy for congestive heart failure and, thus, it encompasses administration of MSC to the same or similar patient having cardiac scar tissue as encompassed by the presently pending claims in the light of specification (specification from page 1, line 19 to page 2, line 4). Thus, the claimed invention is prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited reference. Therefore, the claims are properly rejected under 35 U.S.C. 103.

Claims 2, 5 and 7-9 are free from the prior art of record but remain objected to as being dependent upon a rejected base claim.

Response to Arguments

Applicants' arguments filed 12/15/2003 have been fully considered but they are not persuasive.

Regarding the rejection under 35USC 103 applicants argue that WO 99/03973 is published on 28 January 1999 and, thus, it is not a proper prior art reference considering the priority claim of the instant application. However, applicants' provisional application 60/129, 152 is filed on 4/14/1999 which is after the publication date of the cited WO. The other applicants' provisional application 60/094,794 filed on 7/31/1998 does not provide a full support for the instant independent claim 1. The scope of the instant claim 1 is broader and it is drawn to administration of a suspension containing mesenchymal stem cells (MSC). However, the specification and claims of the provisional application 60/094,794 are drawn to administration to a suspension containing MSC that are induced to differentiate, for example: see specification at section summary (page 2, lines 17-21) and see claim 1. Therefore, the cited WO document is proper prior art reference. As applied to the instant claims it has been established that the instant claims 1, 4, 6, 10 and 11 are not fully supported by the provisional application 60/094,794. The instant claims 2, 5 and 7-9 are fully supported by the provisional application 60/094,794 filed on 7/31/1998.

With respect to the rejected claims applicants argue that the cited prior art does not indicate the scar tissue as a particular site of MSC injection. However, although the particular example in the disclosure cited WO demonstrates a normal animal model (page 8, lines 25-30), the cited WO document also teaches administration of MSC into the damaged myocardium. The damaged myocardium encompasses the presence of scar tissue as explained above. Applicants appear to argue that the cited document does not provide reasonable expectation that the mesenchymal stem cell could improve heart function of damaged myocardium including scar tissue. This argument is not found particularly convincing because the cited document teaches

that the MSC are modified to express proteins of importance for differentiation including myogenic factors (page 4, lines 10-14) and that the MSC are applied together with a carrier so that they become fully developed cardiomyocytes (page 4, par. 1). Moreover, it appears from the applicants' specification that administration of primary MSC cultures or of cultured MSC into the damaged/scar tissue does not affect the heart function (page 23, lines 6-7).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Vera Afremova

AU 1651

March 18, 2004

V. Afremova

VERA AFREMOVA

PATENT EXAMINER